

What is claimed is:

1. A method of inhibiting rejection of a solid organ transplant in a subject having a transplanted tissue comprising:

5 a) administering an alkylating agent to the subject; and
b) subsequently administering T cell depleted bone marrow cells to the subject at approximately the same time as the solid organ transplant,
thereby inhibiting rejection of the solid organ or tissue/cellular transplant.

10 2. The method of claim 1, wherein the alkylating agent is busulfan.

15 3. The method of claim 1 further comprising the step of administering to the subject an immunosuppressive composition that blocks T cell costimulatory signals in the subject.

20 4. The method of claim 3, wherein the immunosuppressive composition comprises a combination of a first ligand that interferes with binding of CD28 to either CD80 or CD86, and a second ligand that interferes with binding of CD154 to CD40.

25 5. The method of claim 4, wherein the first ligand is a soluble CTLA4 molecule.

6. The method of claim 4, wherein the first ligand is CTLA4-Ig.

7. The method of claim 4, wherein the second ligand is an anti-CD154 mAb.

25 8. The method of claim 4, wherein the first ligand is a soluble CTLA4 molecule and the second ligand is an anti-CD154 mAb.

30 9. A method for establishing mixed hematopoietic chimerism in a subject having a transplanted tissue comprising:

a) administering T cell depleted bone marrow cells to the subject;
b) administering an alkylating agent to the subject; and

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c) administering an immunosuppressive composition that blocks T cell costimulatory signals in the subject,
thereby establishing hematopoietic chimerism in the subject.

5 10. The method of claim 9, wherein the alkylating agent is busulfan.

11. The method of claim 9, wherein the immunosuppressive composition comprises a combination of a first ligand that interferes with binding of CD28 to either CD80 or CD86, and a second ligand that interferes with binding of CD154 to CD40.

10 12. The method of claim 11, wherein the first ligand is a soluble CTLA4 molecule.

13. The method of claim 11, wherein the first ligand is CTLA4-Ig.

15 14. The method of claim 11, wherein the second ligand is an anti-CD154 mAb.

15 15. The method of claim 11, wherein the first ligand is a soluble CTLA4 molecule and the second ligand is an anti-CD154 mAb.

20 16. The method of claim 9, wherein the method inhibits rejection of an organ or tissue transplanted into the subject.

17. The method of claim 9, wherein the T cell depleted bone marrow is administered in at least two doses.

25 18. A method for establishing mixed hematopoietic chimerism in a subject having a transplanted tissue comprising:
a) administering T cell depleted bone marrow cells to the subject;
b) administering an immunosuppressive composition that blocks T cell costimulatory signals in the subject; and
c) administering busulfan to the subject,

thereby establishing mixed hematopoitic chimerism in the subject.

19. The method of claim 18, wherein the immunosuppressive composition comprises a combination of a first ligand that interferes with binding of CD28 to either CD80 or CD86, and a second ligand that interferes with binding of CD154 to CD40.
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20. The method of claim 19, wherein the first ligand is a soluble CTLA4 molecule.
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21. The method of claim 19, wherein the first ligand is CTLA4-Ig.
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22. The method of claim 19, wherein the second ligand is an anti-CD154 mAb.
24. A method for treating hemoglobinopathy in a subject by establishing hematopoietic chimerism by the method of claim 9, or 18.
25. The method of claim 24, wherein hemoglobinopathy is beta-thalassemia.
26. The method of claim 24, wherein the hemoglobinopathy is sickle cell disease.
27. The method of claim 1, 9, or 18, wherein the transplanted tissue is a solid organ or tissue/cellular transplant.
28. The method of claim 9 or 18, wherein steps (b) and (c) are concurrent.
29. The method of claim 9 or 18, wherein steps (b) and (c) are subsequent to step (a).
30. The method of claim 2, 10 or 18, wherein the busulfan is administered within one day prior to the solid organ or tissue/cellular transplant.
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31. The method of claim 2, 10 or 18, wherein the busulfan is administered within twelve hours prior to the solid organ or tissue/cellular transplant.

5 32. The method of claim 2, 10 or 18, wherein the busulfan is administered within six hours prior to the solid organ or tissue/cellular transplant.

33. The method of claim 1, 9, or 18, wherein the transplanted tissue is a skin graft.

10 34. A method of reducing rejection of an organ transplant in a subject in need thereof comprising:
a) administering a first dose of T cell depleted bone marrow cells and an immunosuppressive composition to a subject;
b) placement of an organ or tissue/cellular transplant to the subject;
c) administering busulfan to the subject; and
d) administering a second dose of T cell depleted bone marrow cells and an immunosuppressive agent,
thereby reducing rejection of the organ or tissue/cellular transplant.

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20 35. The method of claim 34, wherein the immunosuppressive agent is a combination of a first ligand that interferes with binding of CD28 to either CD80 or CD86, and a second ligand that interferes with binding of CD154 to CD40.

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36. The method of claim 35, wherein the first ligand is a soluble CTLA4 molecule.

37. The method of claim 35, wherein the first ligand is CTLA4-Ig.

38. The method of claim 35, wherein the second ligand is an anti-CD154 mAb.

30 39. The method of claim 35, wherein the first ligand is a soluble CTLA4 molecule and the second ligand is an anti-CD154 mAb.

40. The method of claim 8, 15, 23 or 39, wherein soluble CTLA4 is CTLA4Ig, and the antibody that binds CD154 is MR1.

41. The method of claim 8, 15, 23 or 39, wherein soluble CTLA4 is CTLA4Ig, and the antibody that binds CD154 is selected from a group consisting of ATCC HB11809, HB 11815, HB11816, HB 11817, HB 11819 HB 11821, and HB 11822.

42. A method of inhibiting rejection of a solid organ transplant in a subject having a transplanted tissue comprising

10 a) administering T cell depleted bone marrow cells;

 b) administering busulfan to the subject; and

 c) administering CTLA4Ig and a monoclonal antibody MR1 to the subject, thereby inhibiting rejection of the solid organ or tissue/cellular transplant.

15 43. A method of inhibiting rejection of a solid organ transplant in a subject having a transplanted tissue comprising

 a) administering T cell depleted bone marrow cells;

 b) administering busulfan to the subject; and

 c) administering CTLA4Ig and a monoclonal antibody consisting of ATCC

20 HB11809, HB 11815, HB11816, HB 11817, HB 11819 HB 11821, and HB 11822, to the subject, thereby inhibiting rejection of the solid organ or tissue/cellular transplant.